SYNOPSIS

INN : FEXOFENADINE

Study number : M016455I/1005

Study title : A multicenter study to assess the safety and pharmacokinetics of open-label 30 mg single dose fexofenadine hydrochloride oral suspension (6 mg/mL) in pediatric subjects 2 to 5 years of age

CSR date : 19 September 2005

The study results and synopsis are supplied for informational purposes only.

Not all of the study results have necessarily been reviewed by the Regulatory Authorities.

The decision to prescribe and take a product should always be made on the basis of the most recent version of the product information and product package insert in the country of prescription.
# STUDY SYNOPSIS

<table>
<thead>
<tr>
<th>Study number</th>
<th>M016455I/1005</th>
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<tbody>
<tr>
<td><strong>Title</strong></td>
<td>A multicenter study to assess the safety and pharmacokinetics of open-label 30 mg single dose fexofenadine hydrochloride oral suspension (6 mg/mL) in pediatric subjects 2 to 5 years of age</td>
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<tr>
<td><strong>Investigator(s), study site(s)</strong></td>
<td>Multicenter study, 6 study sites in the US</td>
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<tr>
<td><strong>Study duration and dates</strong></td>
<td>16 March 2005 to 17 April 2005</td>
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### Objectives

The primary objective of this study was to characterize the pharmacokinetic behavior of a single dose of 30 mg fexofenadine HCl administered as an oral suspension (fexofenadine HCl 6mg/mL) in pediatric subjects with allergic rhinitis (AR) who were 2 to 5 years of age.

The secondary objective of this study was to evaluate the safety and tolerability of a single dose of 30 mg fexofenadine HCl administered as an oral suspension (fexofenadine HCl 6 mg/mL) in pediatric subjects with AR who were 2 to 5 years of age.

### Study design

This was a multicenter, open-label, single-dose pharmacokinetic study conducted at 6 study sites in the US.

### Number of subjects planned

Forty-eight (48) subjects were planned for enrollment into this study.

### Inclusion criteria

- Pediatric subjects 2 to 5 years (2 to ≤5 years) years of age whose physician has determined them to be a candidate for antihistamine therapy (including prescription antihistamines, over-the-counter antihistamines, and antihistamines in a combination product) for the treatment of allergic rhinitis

  or

- Pediatric subjects 2 to 5 years (2 to ≤5 years) years of age who have tolerated a therapeutic course of antihistamine therapy for the treatment of allergic rhinitis without adverse effects.

### Treatments

Single-dose 30-mg fexofenadine HCl oral suspension (6 mg/mL).
Pharmacokinetic data
Blood samples were collected prior to dosing (predose) and at 1, 2, 3, 4, 6, 8, 12, and 24 hours following study drug administration. Plasma samples were analyzed by liquid chromatography/tandem mass spectrometry to determine fexofenadine concentration. Pharmacokinetic parameters included \( C_{\text{max}} \), \( t_{\text{max}} \), \( \text{AUC}(0-\text{last}) \), and were determined from fexofenadine plasma concentrations by noncompartmental analysis.

Pharmacodynamic data
Not applicable.

Efficacy data
Not applicable.

Safety data
Safety was evaluated on the basis of physical examinations, adverse events reported and observed, electrocardiogram (ECG) parameters, and vital signs (body temperature, noncrying heart and respiratory rates, and blood pressure) and clinical laboratory data.

Quality-of-life data
Not applicable

Health economic data
Not applicable

Statistical procedures
Descriptive statistics (N, mean, SD, CV, median, minimum, and maximum) were summarized for the plasma concentration data at each planned sampling time point and for the derived pharmacokinetic parameters.

Interim analysis
No interim analysis was performed for this study.

Results - Study subjects and conduct
A total of 50 subjects were enrolled and received study medication. All 50 completed the study according to protocol. The mean age of the subjects was 3.5 ± 1.1 years, 26 (52%) were male and 24 (48%) were female. Subject height averaged 103 ± 8.4 cm and weight averaged 17.6 ± 3.6 kg. Twenty-nine (58%) were white, 9 (18%) were black, 6 (12%) were multiracial, and 6 (12%) were other races.

Results - Pharmacokinetics
The mean \( C_{\text{max}} \) and \( \text{AUC}(0-\text{last}) \) values after administration of 30 mg dose of the fexofenadine HCl suspension to children 2 to 5 years of age are 224 ng/mL and 898 ng•h/mL respectively. The median \( t_{\text{max}} \) value was 1 h. The terminal elimination phase had less than three concentration time points and therefore, \( \lambda_z \), \( t_{1/2} \), \( \text{AUC}(0-\infty) \) and \( \text{CL}_{\text{po}} \) were not estimated for any subject.
Mean plasma fexofenadine pharmacokinetic parameters after administration of single 30 mg dose of fexofenadine HCl suspension to children aged 2 to 5 years

<table>
<thead>
<tr>
<th></th>
<th>C&lt;sub&gt;max&lt;/sub&gt; (ng/mL)</th>
<th>t&lt;sub&gt;max&lt;/sub&gt; (h)</th>
<th>AUC (0-last) (ng·h/mL)</th>
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<tbody>
<tr>
<td>n</td>
<td>50</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Mean</td>
<td>224</td>
<td>1.0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>898</td>
</tr>
<tr>
<td>Range</td>
<td>110 – 437</td>
<td>1.0 – 4.0</td>
<td>459 - 1966</td>
</tr>
<tr>
<td>CV%</td>
<td>39.3</td>
<td>53.3</td>
<td>34.3</td>
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</table>

<sup>a</sup> t<sub>max</sub> reported as median value

Results - Safety

There were a total of 10 treatment-emergent adverse events (TEAE) reported in 7 (14%) subjects during the study. No treatment-emergent adverse event was reported more than once. There were 2 TEAEs (diarrhea and somnolence) in 2 subjects assessed as possibly related to study medication. With the exception of one case of pyrexia (fever) of moderate intensity, all adverse events reported during the study were mild in intensity and resolved without sequelae prior to study conclusion. There were no serious adverse events or discontinuations from the study due to adverse events.

There were no trends or clinically meaningful changes observed in mean laboratory, vital sign, or ECG data from baseline to poststudy. There were 3 subjects with laboratory values (low absolute neutrophil count) at poststudy, which met the predefined clinically significantly abnormal criterion (CSA), but these were not considered as clinically significant by the investigators. One subject had increased blood pressure, which was reported as a TEAE on study Day 2; the investigator considered this event as not related to study medication.

Conclusions

The pharmacokinetics of fexofenadine were characterized in pediatric subjects 2 to 5 years of age after administration of a single 30 mg dose of fexofenadine HCl oral suspension and the results of this study support the selection of a 30 mg dose of fexofenadine HCl 6 mg/mL, oral suspension in children from 2 to 5 years of age.

Fexofenadine HCl, 6 mg/mL oral suspension, was well tolerated when administered as a single, 30 mg dose to pediatric subjects 2 to 5 years of age.